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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,104	09/28/2005	Thorsten Heinzel	LEDER-15	3483

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
AEDER, SEAN E	
ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,104	HEINZEL ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *5,11-13, 15-21, 2-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10,14,22,23,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 11/16/07 in response to the Office Action of 5/16/07 are acknowledged and have been entered.

Claims 21-28 have been added by Applicant.

Claims 1-28 are pending.

Claims 5 and 15-20 have previously been withdrawn.

Claims 1-4 and 10-18 have been amended by Applicant.

Newly submitted claims 24-26 and newly amended claims 11-13 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Elected Group 1 is drawn to a method for characterization of an HDAC inhibitor or a potential HDAC inhibitor comprising determining in a sample the amount of a molecular marker wherein the sample is derived from cells which have been treated with said HDAC inhibitor or potential inhibitor, while claims 11-13 and 24-26 are drawn to are drawn to diagnostic and/or prognostic methods

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 11-13 and 24-26 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 21 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 1-4, 6-10, 14, 22, 23, 27, and 28 are currently under examination.

The following Office Action contains NEW GROUNDS of rejections necessitated by Amendments.

Objections Withdrawn

The objection to the specification is withdrawn.

Rejections Withdrawn

The rejection of claims 10 and 14 under 35 U.S.C. 101 is withdrawn.

The rejection of claims 1-4, 6-10, and 14 under 35 U.S.C. 112 second paragraph, for reciting "HDAC" or "HDAC-2", is withdrawn.

The rejection of claim 4 under 35 U.S.C. 112 second paragraph, because it is unclear what is meant by "is not restricted to", is withdrawn.

The rejection of claims 10 and 14 under 35 U.S.C. 112 second paragraph, for not reciting steps involved in a method/process, is withdrawn. However, a new rejection of claims 10 and 14 under 35 U.S.C. 112 second paragraph necessitated by amendments, for not reciting steps involved in a method/process, is set-forth below.

The rejection of claims1-4 and 6-10 under 35 U.S.C. 112 first paragraph, for failing to comply with the written description requirement, is withdrawn.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and dependent claims 2-4 and 6-9 remain rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps, for the reasons stated in the Office Action of 5/16/07 and for the reasons set-forth below.

The Office Action of 5/16/07 contains the following text:

"Claim 1 recites a method for characterizing an HDAC inhibitor or a potential HDAC inhibitor comprising determining the amount of a molecular marker in a sample derived from cells which have been treated with said HDAC inhibitor or a potential HDAC inhibitor; however, the claims do not indicate what specific result would be indicative of what specific characterization. Thus, there is a missing step involving correlating some type of result to some type of characterization. See MPEP § 2172.01."

In the Reply of 11/16/07, Applicant amended claim 1 but did not specifically address this rejection with arguments.

The amendments to the claims and the arguments found in the Reply of 11/16/07 have been carefully considered, but are not deemed persuasive. It remains unclear what result would be indicative of what specific characterization. Thus, there is a missing step involving correlating some type of result to some type of characterization.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-10, and 14 remain rejected and newly added claims 22 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Macleod et al (WO 00/71703 A2; 11/30/00), for the reasons stated in the Office Action of 5/16/07 and for the reasons set-forth below.

The Office Action of 5/16/07 contains the following text:

"Macleod et al teaches a molecular marker, HDAC-2, which is encoded by instant SEQ ID NO:5 (see attached sequence comparison). Further, Macleod et al teaches a method for the characterization of an HDAC inhibitor or a potential HDAC inhibitor comprising using an antibody specific for HDAC-2 polypeptide to determine in a sample the amount of HDAC-2 polypeptide, where the sample is derived from cells which have been treated with said HDAC inhibitor or potential HDAC inhibitor (Example 3, in particular). Macleod et al further teaches a method wherein said sample is derived from a tissue affected by a disorder (Example 3 and page 2, in particular). Macleod et al further teaches a method wherein said disorder, bladder cancer (the T24 cells of Example 3), is not restricted to the group of disorders listed in instant claim 4. Macleod et al further teaches a method wherein HDAC-2 polypeptide is determined by Western blotting (see Example 3, in particular). Macleod et al further teaches a method wherein inhibitors are selected by the ability to inhibit the expression of HDAC-2 polypeptide (see Example 3, in particular). Macleod et al further teaches a method comprising the step of determining in a reference sample the amount of said molecular marker wherein the reference samples is derived from cells which have not been treated with said HDAC inhibitor or potential HDAC inhibitor (see Example 3, in particular)."

In regards to newly added claim 28, it is noted that the HDAC inhibitor or potential HDAC inhibitor taught by Macleod et al, which inhibits HDAC expression would

interfere with the catalytic activity of HDAC since a lack of HDAC would result in a lack of HDAC catalytic activity.

In the Reply of 11/16/07, Applicant argues that Macleod et al fails to mention any inhibitor or any HDAC inhibitor which is capable of effecting the modulating the expression of the molecular markers in a manner described in Applicant's claims. Applicant further states that one of skill in the art would recognize that Macleod's method of genetic manipulation of protein levels using antisense technology is distinct from Applicant's disclosed technique of modulation of enzyme activity using chemical (small molecule) inhibitors. Applicant further indicates that the pending claims are drawn to a method comprising the characterization of an inhibitor which modulates the catalytic activity of HDAC. Applicant further states that there is no mention in Macleod that antisense molecules interfere with the catalytic activity of HDAC protein.

The arguments found in the Reply of 11/16/07 have been carefully considered, but are not deemed persuasive. In regards to the argument that Macleod et al fails to mention any inhibitor or any HDAC inhibitor which is capable of effecting the modulating the expression of the molecular markers in a manner described in Applicant's claims, the entire document of Macleod et al (entitled "Inhibition of Histone Deacetylase") teaches HDAC inhibitors which effect the modulating the expression of HDAC protein in the manner described in the claims. For instance, Applicant is directed to the Abstract of Macleod et al, which teaches: "...The invention also relates to compositions comprising antisense oligonucleotides and methods of using the same to inhibit a

histone deacetylase. Also disclosed are methods for identifying a histone deacetylase involved in induction of cell proliferation, and methods for identifying compounds that interact with and reduce the enzymatic activity of such a histone deacetylase". Further, Applicant is directed to Example 3 "Inhibitor of Histone Deacetylase Protein Expression With Second Generation Antisense Oligonucleotides" (see page 26). Inhibitors taught by Macleod et al in Example 3, such as MG2628 and MG2836, are capable of effecting the modulating the expression of the molecular markers in a manner described in Applicant's claims.

In regards to the argument that one of skill in the art would recognize that Macleod's method of genetic manipulation of protein levels using antisense technology is distinct from Applicant's disclosed technique of modulation of enzyme activity using chemical (small molecule) inhibitors, the instant claims encompass methods using inhibitors such as those taught by Macleod et al for the reasons discussed above.

In regards arguments that the pending claims are drawn to a method comprising the characterization of an inhibitor which modulates the catalytic activity of HDAC, only newly added claim 28 recites a method wherein the HDAC inhibitor or potential HDAC inhibitor interferes with "the catalytic activity" of HDAC. It is further noted that all the pending claims require that the HDAC inhibitor or potential HDAC inhibitor is characterized by an ability to alter HDAC expression. Clearly, the second generation antisense oligonucleotides taught by Macleod et al would decrease HDAC expression and said decrease in HDAC expression would lead to a decrease in HDAC catalytic activity since a lack of HDAC would result in a lack of HDAC catalytic activity.

In regards to the argument that there is no mention in Macleod that antisense molecules interfere with the catalytic activity of HDAC protein, Example 4 of Macleod et al teaches how antisense molecules interfere with the catalytic activities of HDAC protein required to induce proliferation (see pages 27-28, in particular). Further, the ability of said antisense molecules to interfere with the catalytic activity of HDAC by reducing expression of HDAC protein is an inherent characteristic of said antisense molecules.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 14, 23, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Amended claim 10 and dependent claims 14, 23, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are drawn to methods for profiling HDAC inhibitors or potential HDAC inhibitors comprising contacting a cell with an HDAC inhibitor or potential HDAC inhibitor and determining the amount of HDAC protein in the presence and absence of said inhibitor;

however, the claims do not distinctly point-out or claim how a particular result is to create a profile. The omitted steps are: correlating particular results to the development of a profile.

Newly added claims 23 and 27 recite the limitation "the disease" in reference to claim 10. There is insufficient antecedent basis for this limitation in the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **NEW MATTER** rejection.

Claim 28 recites a method wherein an HDAC inhibitor or potential HDAC inhibitor interferes with "the catalytic activity" of HDAC. Descriptions of methods wherein an HDAC inhibitor or potential HDAC inhibitor interferes with "the catalytic activity" of HDAC are not found in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the invention was filed, had possession of the claimed invention.

Summary

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

/Misook Yu/
Primary Examiner, 1642